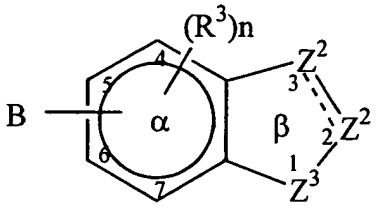
AMENDMENTS TO THE CLAIMS

1. (Previously Amended) A compound of the formula:



(1)

and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein

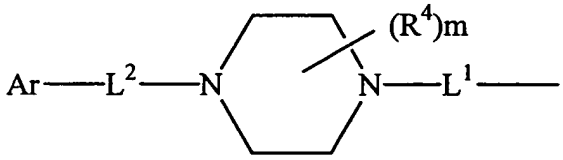
⩫ represents a single or double bond;

B is $-W_i-COX_jY$ wherein Y is COR^2 or an isostere thereof and R^2 is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;

each R^3 is independently a noninterfering substituent, where n is 0-3;

Z^3 is NR^7 or O; wherein R^7 is H or a noninterfering substituent;

one Z^2 is CA or CR^8A and the other is CR^1, CR^1_2, NR^6 or N wherein each R^1, R^6 and R^8 is independently hydrogen or noninterfering substituent; wherein A is:



Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused carbocyclic or heterocyclic aromatic ring;

each R^4 is independently a noninterfering substituent where m is 0-4;

each of L^1 and L^2 is a linker; and

the distance between the atom of Ar linked to L^2 and the center of the β ring is no more than 24Å.

2. (Original) The compound of claim 1 wherein B is -COXjCOR^2, and

wherein R^2 is H, or is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, CN, COOR, $CONR_2$, COR, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, or

wherein R^2 is OR, NR_2, SR, $NRCONR_2$, $OCONR_2$, or $NRSO_2NR_2$, wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, and wherein two R attached to the same atom may form a 3-8 member ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined; and

X, if present, is alkylene.

3. (Original) The compound of claim 1 wherein Y is an isostere of COR^2.

4. (Original) The compound of claim 3 wherein Y is tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole.

5. (Original) The compound of claim 1 wherein each of i and j is 0.

6. (Original) The compound of claim 2 wherein j is 0.

7. (Original) The compound of claim 1 wherein Z^3 is NR^7.

8. (Original) The compound of claim 7 wherein R^7 is H or is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO_2R, RCO, COOR, alkyl-COR, SO_3R, $CONR_2$,

SO_2NR_2, CN, CF_3, NR_2, OR, alkyl-SR, alkyl-SOR, alkyl-SO_2R, alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl-$CONR_2$, or R_3Si, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof.

9. (Original) The compound of claim 8 wherein R^7 is H, or is optionally substituted alkyl, or acyl.

19, (Canceled)

11. (Original) The compound of claim 1 wherein L^1 is CO, CHOH or CH_2.

12. (original) The compound of claim 11 wherein L^1 is CO.

13-14. (Canceled)

15. (Original) The compound of claim 1 wherein L^2 is alkylene (1-4C) or alkenylene (1-4C) optionally substituted with a moiety selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two substituents on L^2 can be joined to form a non-aromatic saturated or unsaturated ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety.

16. (Original) The compound of claim 15 wherein L^2 is unsubstituted alkylene.

17. (Original) The compound of claim 15 wherein L^2 is unsubstituted methylene, methylene substituted with alkyl, or -CH=.

18. (Original) The compound of claim 1 wherein Ar is optionally substituted with 0-5 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

19. (Original) The compound of claim 18 wherein Ar is optionally substituted phenyl.

20. (Original) The compound of claim 19 wherein said optional substitution is by halo, OR, or alkyl.

21. (Original) The compound of claim 20 wherein said phenyl is unsubstituted or has a single substituent.

22. (Original) The compound of claim 1 wherein R^4 is selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R^4 on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R^4 is =O or an oxime, oximeether, oximeester or ketal thereof.

23. (Original) The compound of claim 22 wherein each R^4 is halo, OR, or alkyl.

24. (Original) The compound of claim 23 wherein m is 0, 1, or 2.

25. (Original) The compound of claim 24 wherein m is 2 and both R^4 are alkyl.

26. (Original) The compound of claim 1 wherein each R^3 is halo, alkyl, heteroalkyl, OCOR, OR, NRCOR, SR, or NR_2, wherein R is H, alkyl, aryl, or heteroforms thereof.

27. (Original) The compound of claim 26 wherein R^3 is halo or alkoxy.

28. (Original) The compound of claim 27 wherein n is 0, 1 or 2.

29. (Original) The compound of claim 1 wherein L^1 is coupled to the β ring at the 5-position.

30. (Original) The compound of claim 1 wherein Z^2 at position 3 is CA or CH^1A.

31. (Original) The compound of claim 30 wherein the Z^2 at position 2 is CR^1 or CR^1_2.

32. (Original) The compound of claim 31 wherein R^1 is hydrogen, or is alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R^1 can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

33. (Original) The compound of claim 32 wherein each R^1 is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR_2, SR, NRCOR, alkyl-OOR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or heteroforms thereof.

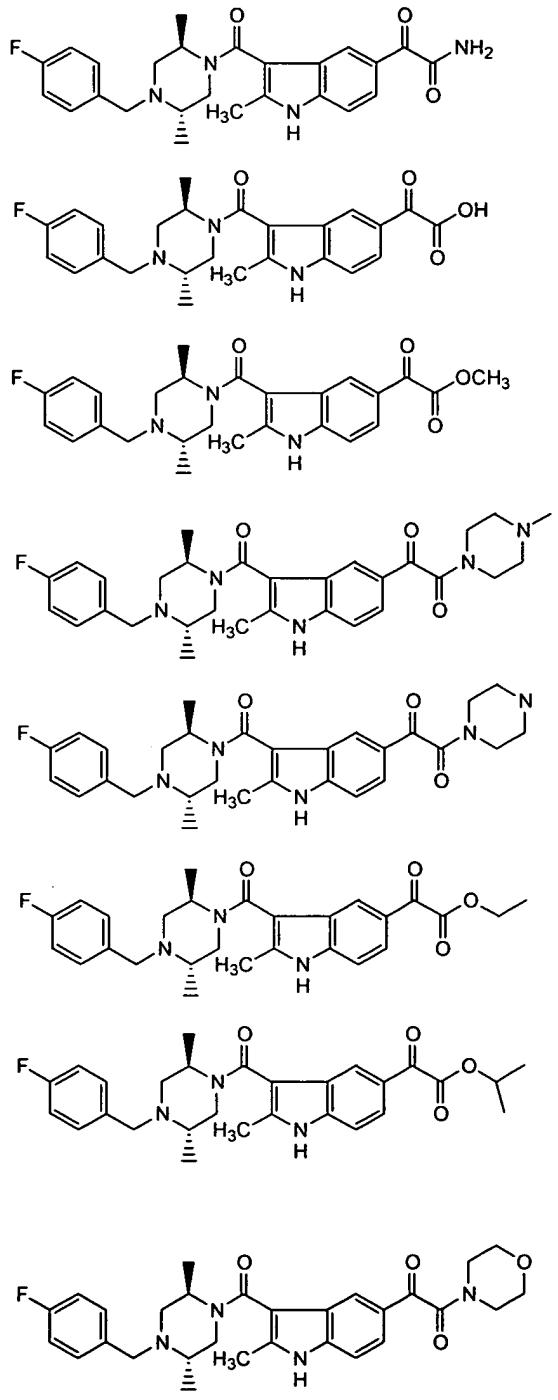
34. (Original) The compound of claim 30 wherein Z^2 at position 2 is N or NR^6.

35. (Original) The compound of claim 34 wherein R^6 is H, or alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO_2R, RCO, COOR, alkyl-COR, SO_3R, $CONR_2$, SO_2NR_2, CN, CF_3, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof.

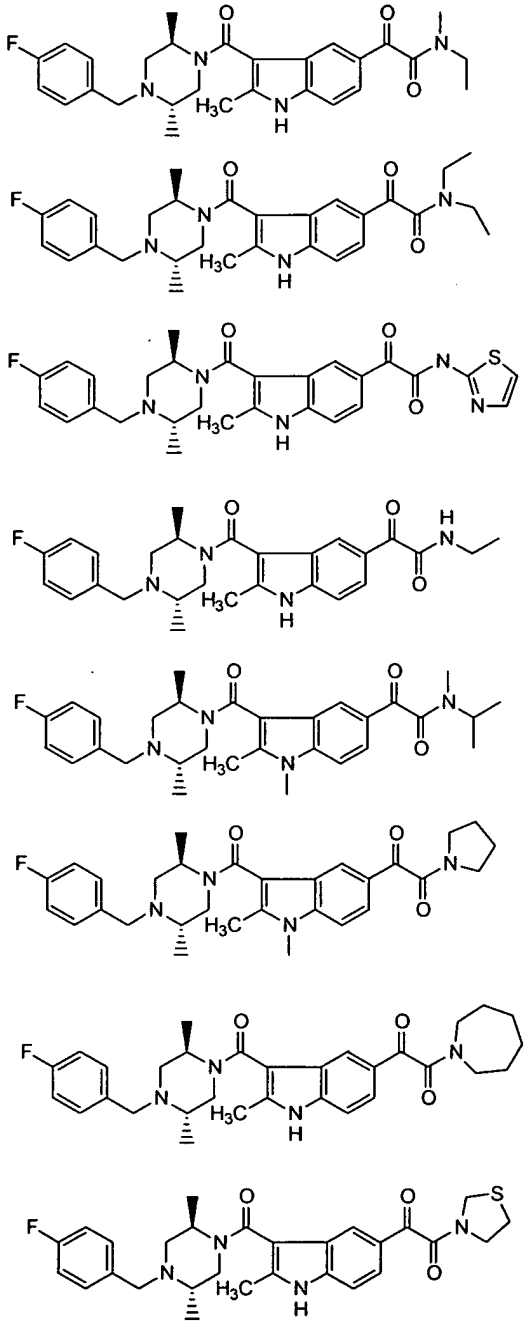
36. (Original) The compound of claim 1 wherein  represents a double bond.

37. (Original) The compound of claim 1 wherein the distance between the atom on Ar linked to L^2 and the center of the β ring is 7.5-11Å.

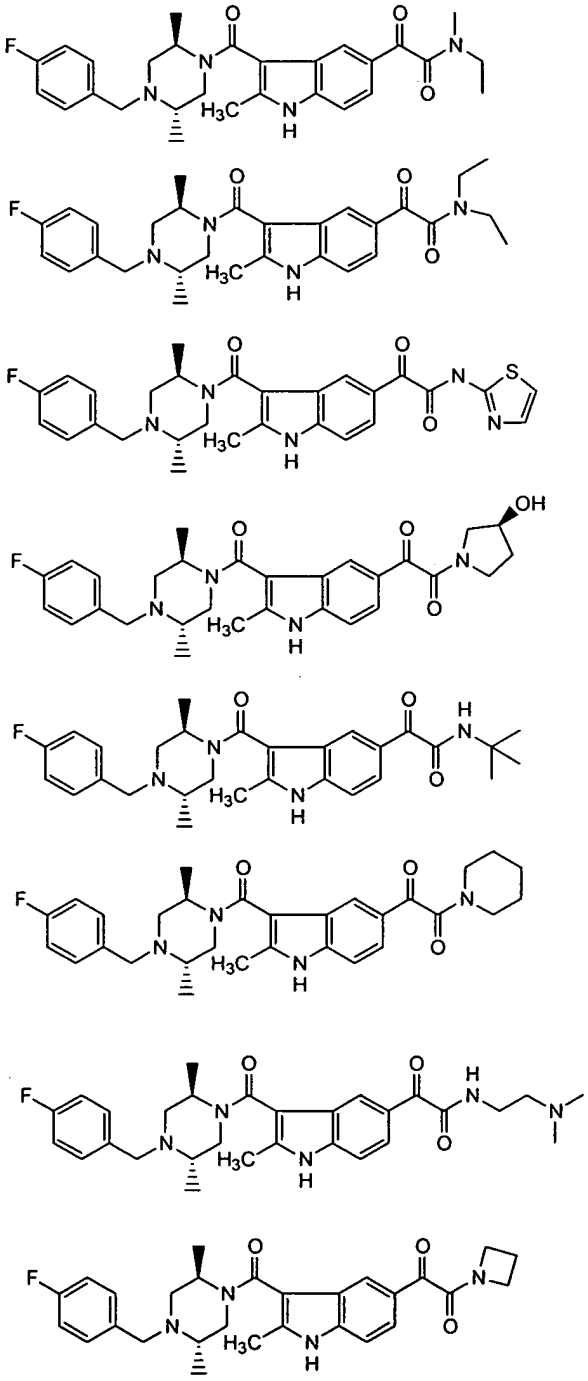
38. (Currently Amended) The compound of claim 1 wherein the compound of formula (1) is selected from the group consisting of:



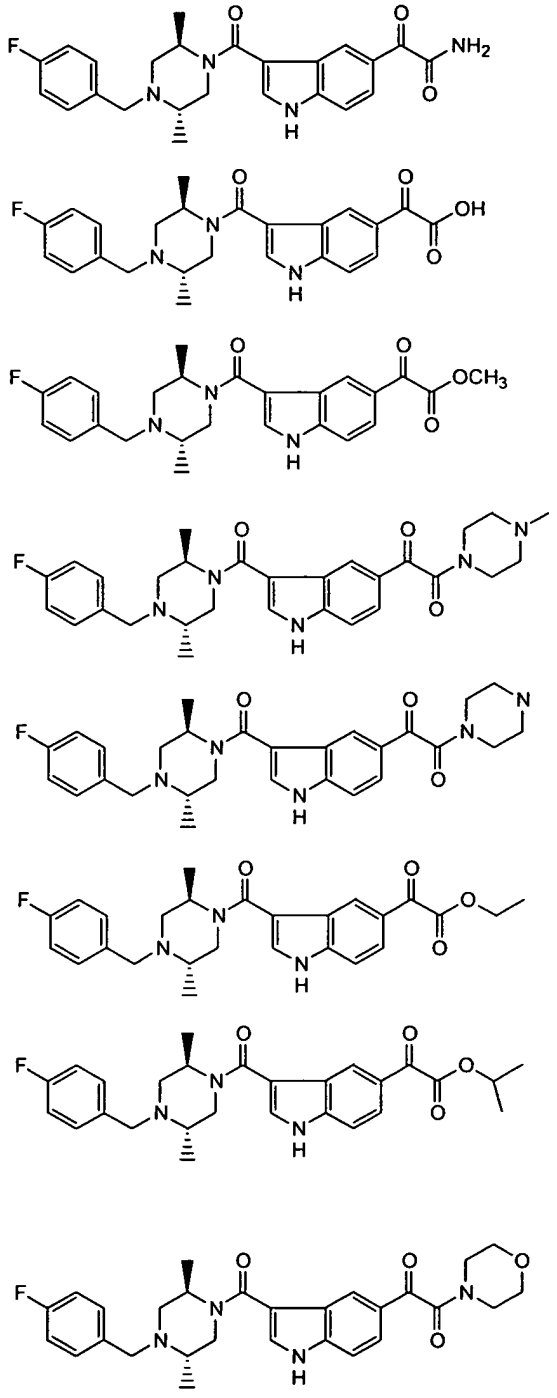
[List -2A]



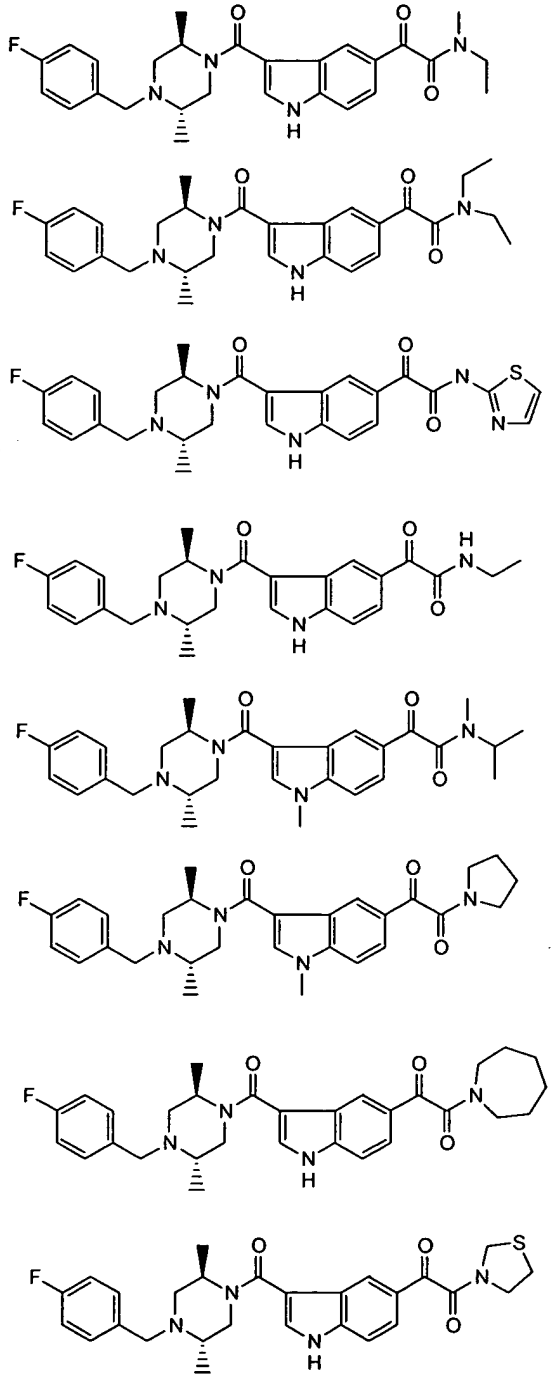
[List -2B]



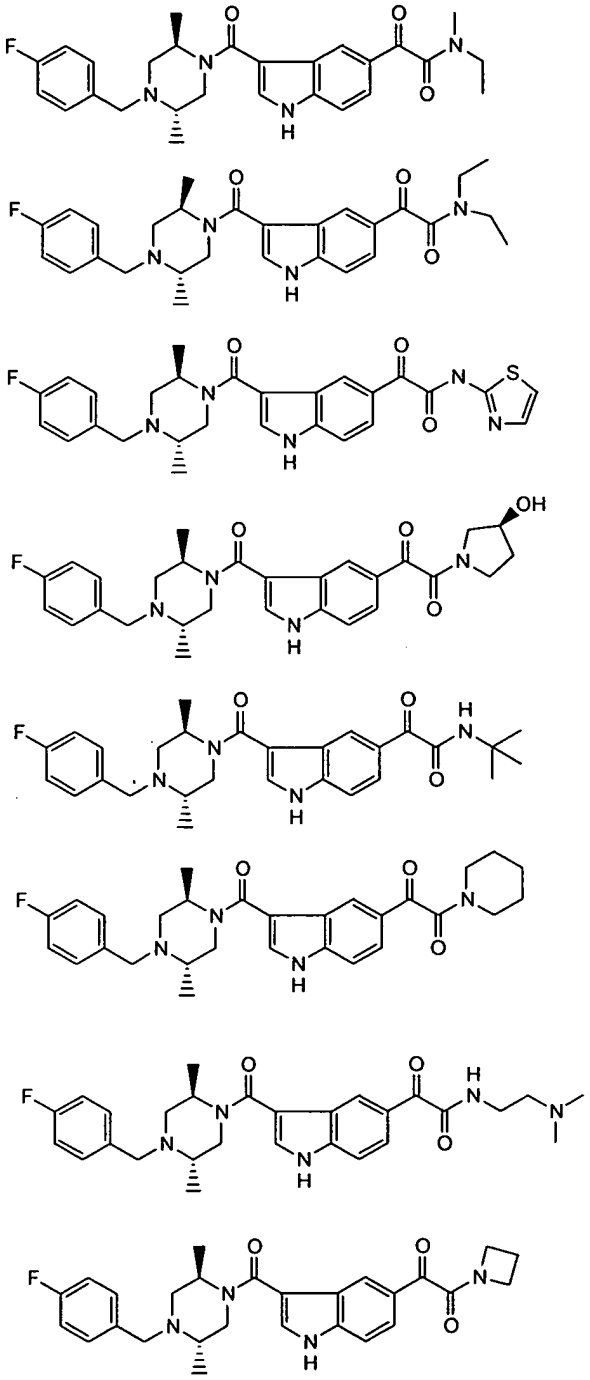
[List -2C]



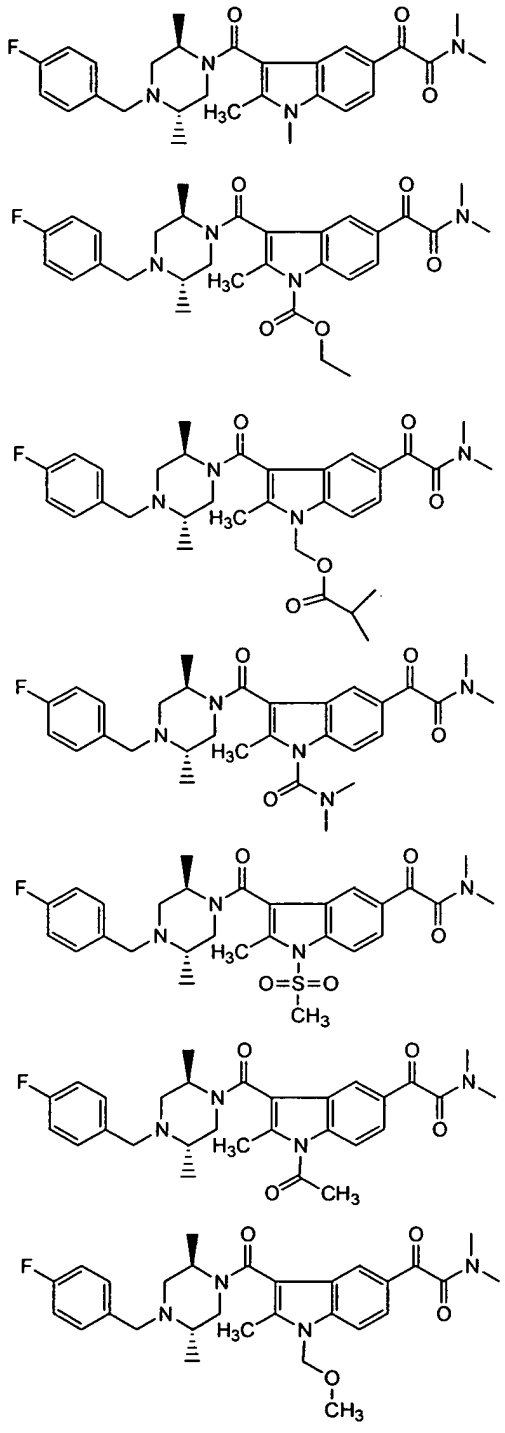
[List -2D]



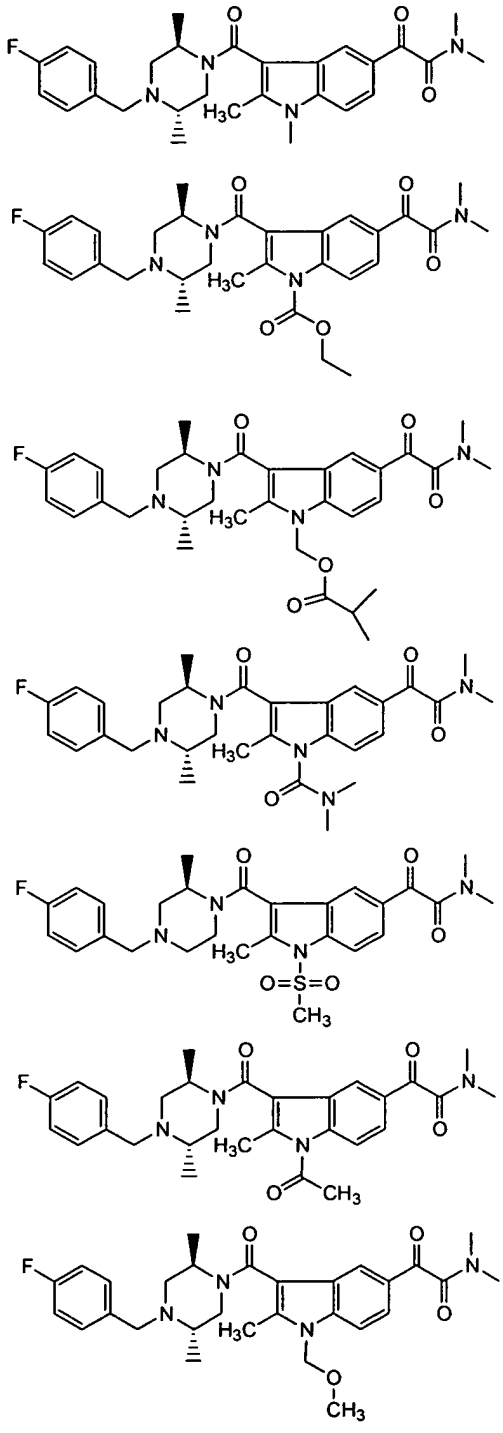
[List -2E]



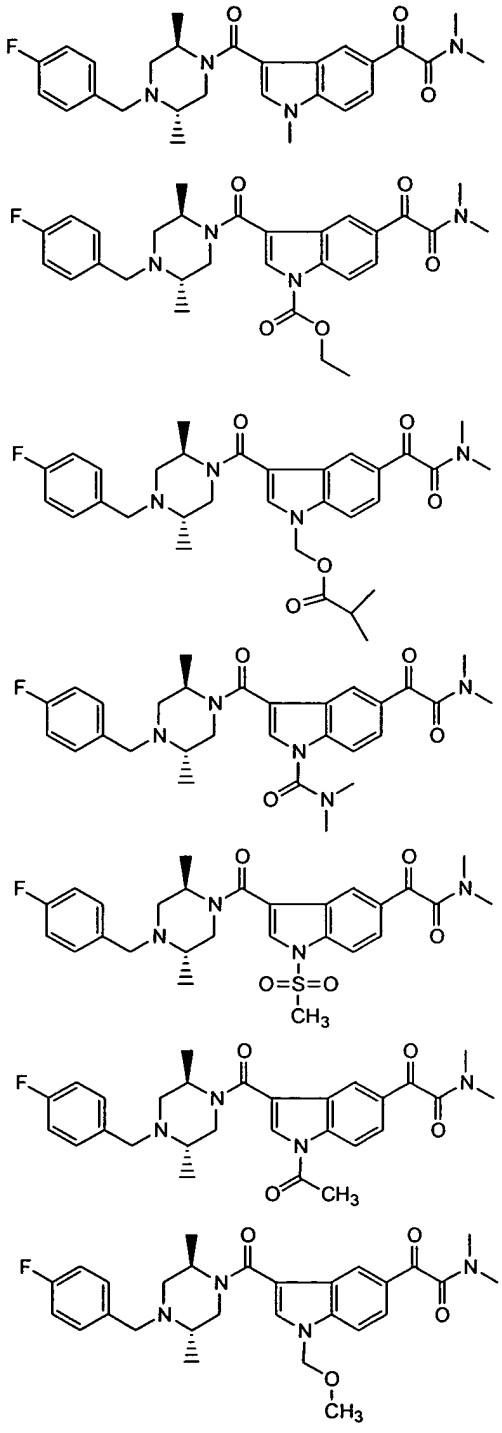
[List -2F]



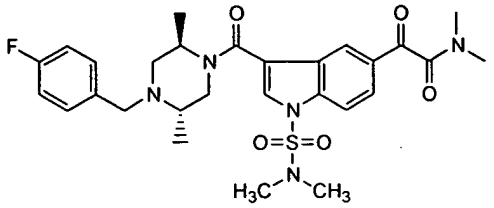
[List -2G]

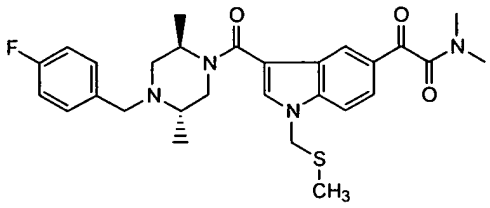


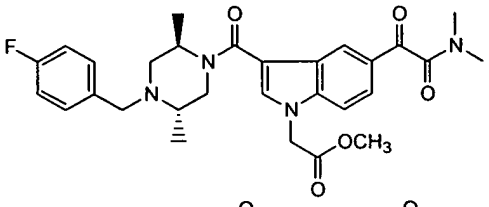
[List -2H]

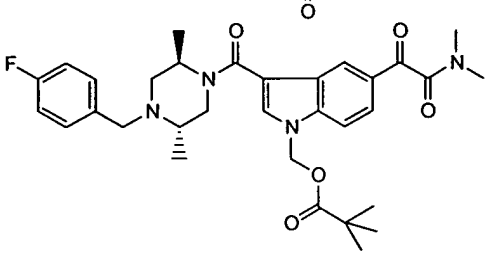


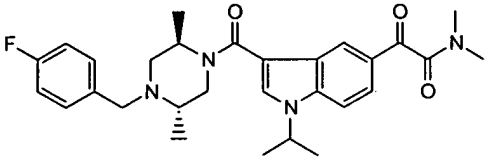
[List -2I]

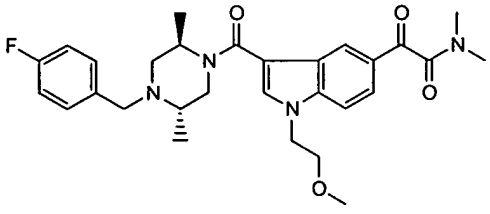












[List -2J]

39. (Previously Amended) A pharmaceutical composition which composition comprises a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof in admixture with at least one pharmaceutically acceptable carrier.

40. (Original) The composition of claim 39 which further contains an additional therapeutic agent.

41. (Original) The composition of claim 40 wherein said additional therapeutic agent is a corticosteroid, a monoclonal antibody, or an inhibitor of cell division.

42. (Previously Amended) A method to treat a condition mediated by p38-α kinase comprising administering to a subject in need of such treatment a compound of claim 1 or: a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof.

43. (Original) The method of claim 42 wherein said condition is a proinflammation response.

44. (Currently Amended) The method of claim 43 wherein said proinflammation response is multiple sclerosis, [IBD] inflammatory bowel disease, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, [other arthritic conditions,] sepsis, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, asthma, adult respiratory distress syndrome, reperfusion injury, psoriasis, [restenosis], cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, a bone resorption disease, graft-versus-host reaction, Crohn's Disease, ulcerative colitis, [Alzheimer's] or pyresis.